REMARKS

The Official Action of June 17, 2008 and the art cited therein have been carefully considered. The amendments and remarks herein are considered to be responsive thereto.

I. Status of the Claims

After entry of these amendments, claims 37-43 are pending.

Claim 37 is amended to correct capitalization errors, to delete the definitions of variables "a" and "b", and to correct a typographical error in the word "substituted" in the definition of R^1.

Claim 37 is also amended to overcome an indefiniteness rejection regarding the definition of "R^a" and "R^b". Support for this amendment is found throughout the specification, including on pages 8-9, 22-23, and 46-52.

No new matter is added by these amendments.

II. Objections on formal grounds

Claim 37 is objected to because the word "unsubstituted" is capitalized. Claim 37 has been corrected to address this concern.

Claims 40-42 are objected to as being dependent upon rejected base Claim 39. Applicants believe the remarks herein place base Claim 39 in condition for allowance and therefore request that Examiner withdraw her objection to Claims 40-42.

III. Rejections under 35 USC § 112

Claims 37, 38, and 43 are rejected under 35 USC 112 as being indefinite.

Examiner stated that described variables "a" and "b" in Claim 37 are vague because these variables are not defined on formula I. Claim 37 has been corrected by deleting variables "a" and "b".

Examiner stated that the definitions of "R^a" and "R^b" are indefinite because they are defined with themselves. Accordingly, Applicants have amended the definitions of "R^a" and "R^b" in Claim 37 to address this concern. No new matter has been added.

IV. Rejections under 35 USC § 103(a)

A. Statements of Common Ownership as Required by 35 USC 103(c)

The following statements are made as outlined in MPEP 706.02(l)(2) in order to disqualify references as prior art under 35 USC 103(c).

a. Claims 37-39 and 43 are rejected under 35 USC 103(a) as being unpatentable over Bilodeau et al. (US 6380203 B1). Present application 10/540,784 and U.S. Patent No. 6,380,203 were, at the time the invention of Application 10/540,784 was made, owned by Merck & Co., Inc.

b. Claims 37-39 and 43 are rejected under 35 USC 103(a) as being unpatentable over Bilodeau et al. (US 6235741 B1). Present application 10/540,784 and U.S. Patent No. 6,235,741 were, at the time the invention of Application 10/540,784 was made, owned by Merck & Co., Inc.

c. Claims 37, 38, and 43 are rejected under 35 USC 103(a) as being unpatentable over Bilodeau et al. (US 6245759 B1). Present application 10/540,784 and U.S. Patent No. 6,245,759 were, at the time the invention of Application 10/540,784 was made, owned by Merck & Co., Inc.

d. Claims 37, 38, and 43 are rejected under 35 USC 103(a) as being unpatentable over DeFeo-Jones et al. (US 20020041880 A1). Present application 10/540,784 and U.S. Patent Application Publication 2002/0041880 A1 were, at the time the invention of Application 10/540,784 was made, owned by Merck & Co., Inc.

B. Rejection based on Bellec et al.

Claims 37, 38, and 43 are rejected under 35 USC 103(a) as being unpatentable over Bellec et al. (J. of Heterocyclic Chemistry, 1995, 32(6), 1793-1800). The Examiner states that the claimed invention claims compounds of formula (I) wherein R^2, R^3, and R^5 = hydrogen, R^4 = phenyl, and R^1 = methyl. The Examiner further states that Bellec et al. teaches compounds where R^2 = methyl, R^3 and R^5 = hydrogen, R^4 = phenyl, and R^1 = hydrogen, see Table 1, page 1794, compound 1c of Bellec et al. The Examiner states that "[c]ompounds which are position isomers . . . or homologs . . . are

generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties," citing MPEP 2144.09(II).

However, MPEP 2144.09(VI) explains, "If the prior art does not teach <u>any</u> specific or significant utility for the disclosed compounds, then the prior art is unlikely to render structurally similar claims prima facie obvious in the absence of any reason for one of ordinary skill in the art to make the reference compounds or any structurally related compounds. In re Stemniski, 444 F.2d 581, 170 USPQ 343 (CCPA 1971)."

Bellec et al. does not disclose any pharmaceutical or biological use for the compounds it teaches. The authors merely state that they "have been interested for some time in the chemical and electrochemical reduction of N-heterocyclic compounds." Bellec et al., p. 1793. The only properties described for the disclosed compounds are physical properties such as NMR spectra, polarography data, pH values, and melting points. Thus, the useful properties of the compounds of the present invention (e.g. ability to inhibit/regulate/modulate tyrosine kinase transduction, usefulness for treating tyrosine kinase-dependent diseases and conditions, see specification) could not be "expected" from the teachings of Bellec et al. Bellec et al. does not suggest any reason for one skilled in the art to make the reference compounds or structurally related compounds for pharmaceutical use.

"[I]n cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." Takeda v. Alphapharm, 492 F.3d 1350 (Fed. Cir. 2007). Since the Examiner has not stated any reason that would have led a chemist to modify the compounds of Bellec et al. to arrive at the claimed compounds, a prima facie case of obviousness under 35 USC 103(a) has not been established and Applicants request that the rejection be withdrawn.

V. <u>Double Patenting</u>

A. Rejection over Claims 1-3 of U.S. Patent No. 6,235,741

Claims 37-39 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting over Claims 1-3 of U.S. Patent No. 6,235,741 ('741).

Examiner concedes that the claims of the present application and those of '741 are not identical, but states that the present claims are not patentably distinct because "the '741 patent contains obvious variants of the species embraced by the genus of the instant Application." The Examiner then states that the generic teaching in '741 that R^1 can be alkyl and that "significant overlap at R^4" supports the double-patenting rejection.

The purpose of the doctrine of nonstatutory (obviousness-type) double patenting is to prevent issuance of a patent on claims that are not patentably distinct from the claims of an earlier patent. See Eli Lilly & Co. v. Barr Laboratories, 251 F.3d 955, 968 (Fed. Cir. 2001). Obviousness-type double patenting differs from obviousness under 35 USC 103 in that 103 obviousness compares the claimed subject matter to the prior art, while nonstatutory double patenting compares *claims* in an earlier patent to *claims* in a later patent application. Geneva Pharm. Inc. v. Glaxosmithkline, 349 F.3d 1373, 1378 (Fed. Cir. 2003). "Because nonstatutory double patenting compares earlier and later claims, an earlier patent's disclosure is not available to show nonstatutory double patenting." Id. at 1385. Thus, the Examiner's reference to the teaching of R^1 as alkyl in the '741 patent discloseure is irrelevant to a nonstatutory double patenting rejection because R^1 is not defined as alkyl in the *claims* of '741.

Applicants also assert that claims 37-39 and 43 are patentabely distinct from Claims 1-3 of '741. '741 Claim 1 teaches that R^1 is chosen from "pyridyl, pyrimidyl, thienyl or pyrazinyl, optionally substituted with from one to three members selected from R^a" ('741, column 21, lines 14-16), and R^a is defined as "H, C_{1-10} alkyl, halogen, OH, OC_{1-6}alkyl, NR^7R^8 or phenyl, said OC_{1-6} alkyl is optionally substituted with NR^7R^8" ('741, column 21, lines 25-27). Claim 37 of the instant application discloses that R^1 is C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_8 alkyl, $(C=O)NR^aR^b$, $(C=O)R^c$, $(C=O)OR^c$, or heterocyclyl, wherein the said heterocyclyl group is optionally substituted with at least one substituent selected from C_0-C_6 alkyl-$(C=O)NR^aR^b$, C_0-C_6 alkyl-SO_mR^d, C_0-C_6 alkyl-CO_2R^c, C_1-C_6 alkyl-OR^c, C_1-C_6 alkyl-NR^aR^b, and C_0-C_6 alkyl-$(C=O)$-C_0-C_6 alkyl-OR^c. First, the instant application discloses many R^1 groups that are chemically and structurally distinct from the four named heterocycles of '741

Claim 1. Second, even if R^1 is a heterocycle in compounds of the present application, the optional substituents on said heterocycle are chemically and structurally distinct from the substituents allowed on the R^1 group of '741 Claim 1. Based on the disclosure in '741, one skilled in the art would not have been motivated to make compounds of the present invention wherein a heterocyclic R^1 is substituted with the disclosed substituents. The Examiner has not cited any reason one skilled in the art would have had to make the changes necessary to arrive at the compounds of the present invention, nor why one skilled in the art would have expected that making the necessary modifications would produce tyrosine kinase inhibitors.

Additionally, '741 Claim 1 defines R^4 as phenyl, pyridyl, pyrimidyl, thienyl, or pyrazinyl, optionally substituted with from one to three members selected from R^a, provided that only one of R^3 and R^4 is one of the defined optionally substituted heterocycles and the other is H or C_{1-6} alkyl ('741, column 21, lines 19-23). Contrastingly, instant Claim 37 defines R^4 as C_{6-10} aryl or C_{5-10} heterocyclyl. The instant definition of R^4 is patentably distinct from that in '741 Claim 1 because, inter alia, R^4 cannot be H or alkyl in the instant invention, and the instant invention allows R^4 to be chosen from any C_{6-10} aryl or C_{5-10} heterocyclyl group optionally substituted with an R^a group that can differ significantly from those R^a groups disclosed in '741.

Thus, generic Claim 37 of the instant application is patentably distinct from the claims of the '741 patent because the disclosed R^1, R^a, and R^4 groups are chemically and structurally different. Claims 38 and 43 depend from Claim 37 and are therefore also patentably distinct from '741 Claims 1-3. Claim 43 is also patentably distinct from the claims of '741 because Claim 43 is to a pharmaceutical composition of a compound of Claim 37 and a pharmaceutically acceptable carrier, and '741 does not claim a pharmaceutical composition. Claim 39 is patentably distinct from Claims 1-3 of '741 because the named compounds in instant Claim 39 are chemically and structurally distinct from those claimed in '741, and the Examiner has not given any reason for one skilled in the art to modify the compounds of '741 Claim 3 to arrive at the compounds of instant Claim 39.

B. Rejection over Claims 1-3 of U.S. Patent No. 6,245,759

Claims 37, 38 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 of U.S. Patent No. 6,245,759 ('759). Examiner concedes that the claims of the present application and those of '759 are not identical, but states that the present claims are not patentably distinct because the compound (3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one is obvious over 1-(3-dimethylamino-propyl)-4-(3-thiopen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one, which is named in Claim 2 of '759.

Applicants have amended the definition of R^4 in Claim 37 to exclude pyrididonyl, which modification overcomes the Examiner's rejection. Examiner also expressed a concern that a hydroxypyridine R^4 substituent could tautomerize to give a pyridinonyl group. While Claim 37 does allow R^4 to be pyridyl, Applicants point out that R^4 is optionally substituted with R^b, and the definition of R^b does not include hydroxyl. Thus, there should be no concern regarding tautomerization.

The Examiner also stated that "R^1 can be alkyl, alkenyl and alkynyl, see column 4, lines 15, as taught by the '759 patent." As mentioned above, a nonstatutory obviousness-type rejection cannot be founded on the disclosure of the earlier patent, it must be founded on a comparison between the *claims* of the earlier patent and the *claims* of later application. Thus, the Examiner's reference to the '759 disclosure does not support the rejection.

C. Rejection over Claims 1-3 of U.S. Patent No. 6,380,203

Claims 37-39 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 of U.S. Patent No. 6,380,203 ('203). The Examiner concedes that the conflicting claims are not identical, but states "they are not patentably distinct from each other for the same reason cited in the 103 art rejection above."

In response, Applicants contend that the Examiner's conclusory statement is insufficient to give notice of the reasons for the rejection. MPEP 2141(II) states that an

Examiner must support an obviousness rejection by articulating her findings regarding the Graham factors and explaining her conclusion of obviousness. "35 USC 132 requires that the applicant be notified of the reasons for the rejection of the claim so that he or she can decide how best to proceed." MPEP 2141(II). The Examiner's explanation "for the same reason cited in the 103 art rejection above" does not give the Applicants notice of the factual basis for the rejection. The double patenting rejections based on '741 and '759 were based on specific comparisons of the instant claims to the prior patented claims. Since '741 and '759 claim patentably distinct species from those claimed in '203, it is not clear how the same reasoning can support a rejection over '203. Therefore, the rejection is improper and Applicants request that it be withdrawn.

VI. Conclusion

In light of the amendments and remarks herein Applicants believe the claims are in condition for allowance. The Examiner is respectfully requested withdraw the objections and 35 USC sections 112, 103(a), and nonstatutory obviousness-type double patenting rejections and to contact the undersigned at the number below if this would expedite the allowance.

Respectfully submitted,

By: _____

Sylvia A. Axler
Reg. No. 36,436
Attorney for Applicant(s)
MERCK & CO., INC.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-4909

Date: July 30, 2008